Allergy Abstracts

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From the Allergy Division of
The Jewish Hospital of Brooklyn

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Asthma and Hay Fever

Variations in the Vital-Capacity Measurement in Patients With Bronchial Asthma and Pulmonary Emphysema. Scarrone, L. A., Levin, R., and Barach, A. L.: New England J. Med. **252**: 57, 1955.

The vital capacity of normal subjects and of patients with bronchial asthma and pulmonary emphysema was recorded as a graphic tracing by means of the Benedict-Roth spirometer and also on the McKesson-Scott spirometer. The subjects were told to breathe slowly and steadily into the spirometer after a maximal inspiration. The best of three determinations was recorded as the "slow" vital capacity. After a rest period, a second test was carried out, in which the patients were instructed to exhale as rapidly as possible into the apparatus. The best of three determinations was recorded as the "fast" vital capacity. The difference between the two was calculated according to the formula: slow minus fast vital capacity divided by fast vital capacity. Slow and fast vital-capacities were ascertained in 40 healthy subjects whose average age was 41 years. The difference between the slow and fast capacities in 37 of these subjects was within the range of −5 to +5 per

cent. One patient was in the −5 to −10 per cent range, and two were in the +5 to +20 per cent range. Thirty-five hospitalized patients without cardiopulmonary disease were studied. The mean age of this group was 56 years. Twenty-four, or 69 per cent, fell in the −5 to +5 per cent range. Three were in the −10 to −15 per cent range, 4 in the −5 to −10 per cent range, and 2 each in the +5 to +10 per cent range and +10 to +20 per cent range. Thirty patients with bronchial asthma, without demonstrable chronic emphysema and with an average age of 48 years, were also studied. In this group, 16 (53 per cent) were in the −5 to +5 per cent range. The remainder showed varying degrees of difference in the two types of vital capacity, in some cases as great as 50 per cent. One hundred three tests were performed in 67 patients (average age 60 years) with obstructive pulmonary emphysema with or without demonstrable bronchospasm. In 26 (25 per cent of the total tests), the difference between the two tests was within the −5 to +5 per cent range. The remainder (75 per cent) showed a marked differential between the two vital capacity determinations, the highest being 126 per cent. Although these variations were not correlated with the degree of anatomic change in the lungs as shown on x-ray examination, the greatest divergence appeared to be in the patients with the most advanced emphysema. The causes of this variation are discussed and the necessity for the uniform performance of the vital-capacity determinations is emphasized. E. W.

Prednisone in Allergic Diseases. Feinberg, A. R., and Feinberg, S. M.: J. A. M. A. **160**: 264, 1956.

The effectiveness of prednisone was evaluated in 80 patients with allergic diseases. Of 50 patients with chronic perennial asthma, 41 obtained complete or nearly complete relief of symptoms with adequate doses and 9 had partial relief. Ten patients with seasonal asthma due to pollen or mold allergy were well controlled with prednisone therapy. Among the asthmatics, there were 32 cases of seasonal allergic rhinitis; in all except 5 the nasal symptoms were also controlled by prednisone. Good results were obtained in 1 of 2 patients with perennial allergic rhinitis and in 4 of 6 patients with atopic dermatitis.

Most of the patients obtained improvement from prednisone in doses about one-fifth of those required with cortisone. The initial dose of prednisone varied, in most cases, from 20 to 30 mg. per day; the maintenance dose ranged from 10 to 15 mg. daily. For the control of nasal allergy, higher doses of prednisone were required than for the control of asthma; generalized dermatoses required larger doses than did mild asthma. Asthma complicated by acute bronchial infection necessitated an increase in dosage. The side-effects of prednisone included gastric disturbances, euphoria, increased appetite, overstimulation, and muscle cramps. There were instances of excessive perspiration and urinary frequency. It appeared that prednisone is far less likely than cortisone to lead to fluid retention. M. C.

Dermatology

Nonrecurring Chlorpromazine Dermatitis. Margolis, L. H., Butler, R. N., and Fischer, A.: Arch. Dermat. **72**: 72, 1955.

Of 53 patients receiving chlorpromazine therapy, 7 developed a dermatitis after having been on the drug for periods varying from 9 to 37 days. The eruption was of a maculopapular, erythematous, pruritic character; it was confined to the trunk and extremities, but spared the face, mucous membranes, palms, and soles. In 6 of the cases, the dermatitis quickly cleared when

chlorpromazine was discontinued. One patient. who was taking up to 200 mg. a day, was continued on chlorpromazine in spite of the rash. The dermatitis cleared 12 days later, even though therapy was not interrupted. In 4 patients, treatment was resumed, after the eruption had cleared, with a 10 mg. oral test dose of the drug. This dose was gradually increased until the predermatitis level of dosage was attained. There was no recurrence of the rash. The top dosage in these patients varied from 400 to 800 mg. of chlorpromazine a day. Two patients no longer requiring therapy by the time the rash had appeared tolerated a single 10 mg. test dose without recurrence of the eruption.

The authors also observed that about 25 per cent of all the patients taking chlorpromazine developed, after mild exposures to sunlight, an increased sensitivity to sunlight which was manifested by the repeated occurrence of a fine erythematous eruption. The rash was always confined to the exposed areas and was usually sufficiently mild that discontinuance of the drug was not necessary.

The experience of these workers indicates that the appearance of drug eruptions in patients on chlorpromazine therapy does not necessarily require permanent discontinuance of the drug. It should be withdrawn until the dermatitis has cleared and then may safely be gradually resumed. R. W.

Cross-Sensitivity Between Nickel and Copper. With Remarks On Cross-Sensitivity Between Nickel, Cobalt and Chromates. Epstein, S.: J. Invest. Dermat. **25**: 269, 1955.

A study was made of 32 cases of dermatitis caused by contact with metals in watches, watch bands, spectacle frames, and garters. Patch and/or intracutaneous tests were performed on all patients. The latter test was performed by injecting 0.02 to 0.05 ml. of a sterile 1:40,000 or 1:10,000 solution of nickel sulfate and copper sulfate. A 10 per cent solution of these compounds was used for patch testing. By patch and/or intracutaneous tests, there were 12 positive reactions to copper and nickel, 18 positive reactions to nickel alone, and 2 positive reactions to copper alone. The existence of cross-sensitivity between copper and nickel was suggested by the high percentage of reactions which occurred to both nickel and copper, especially since copper is known to be a poor sensitizer. The significance of these findings was not clear-cut since many nickel-containing alloys are known to contain copper. It was noted that final proof of the existence of cross-sensitivity between the two metals would necessitate experimental sensitization with pure chemicals, as done by Haxthausen with cobalt and nickel. M. C.

Percutaneous Absorption of Hydrocortisone-4-C^{14} in Two Human Subjects. Malkinson, F. D., and Ferguson, E. H.: J. Invest. Dermat. **25**: 281, 1955.

The radioactive steroid, hydrocortisone-4-C^{14}, was applied as a 2.5 per cent ointment to a 39 square centimeter area of normal skin over the flexor aspect of the forearm of 2 hospitalized subjects. Each site was covered with a perforated aluminum eye patch which was taped to the skin for 6 days. During this time, daily 24-hour urine specimens were collected and analyzed for the 17-ketosteroid fraction by means of a radioactive measurement technique. Within 24 hours after application of the ointment, significant radioactivity appeared in the urine of each patient. The peak of radioactive excretion was reached in the second 24-hour period, and then declined by the fourth day to relatively low levels which persisted until the end of the experiment. It appeared that less than 1 per cent of the topically applied hydro-

cortisone-4-C^{14} was excreted in the urine during the 6-day period of the experiment. These findings suggest that following initial percutaneous absorption of hormone and a high excretion rate, a depot of hydrocortisone forms, possibly in the skin, which gradually releases small amounts of hormone for many days. M. C.

Desensitization in Streptomycin Allergy of Nursing Personnel. Jahrmärker, H.: Ärztl. Wchnschr. **10**: 873, 1955 (Abstract, J. A. M. A. **159**: 1494, 1955).

Severe sensitivity to streptomycin developed in 2 nurses who were handling the drug. In one nurse, conjunctivitis and widespread urticaria on the exposed portions of the skin occurred after 5 months of contact. Specific desensitization was attempted by a series of subcutaneous injections of streptomycin, beginning with subthreshold doses. One patient developed a good tolerance to continuous occupational exposure to the drug. It was not possible to desensitize the second patient, who was apparently more sensitive to the drug than the first patient. Success by desensitization apparently depends more on the degree of clinical sensitivity which exists prior to treatment than on the doses used. M. C.

Miscellaneous Allergies

Experimental Allergic Encephalomyelitis After the Excision of the Injection Site of Antigen-Adjuvant Emulsion. Freund, J., and Lipton, M. A.: J. Immunol. **75**: 454, 1955.

Following single intracutaneous injections into guinea pigs of rabbit spinal cord suspension plus complete adjuvant (water-in-paraffin-oil emulsion containing killed mycobacteria), the sites of administration were excised at varying intervals of time. The neurologic symptoms, particularly paralysis, and the histologic evidences of encephalomyelitis were compared in these animals with those of controls in which depot excisions were omitted. If excision of the injected site was delayed for as little as one hour, allergic encephalitis and tuberculin sensitivity developed in a large percentage of these animals. The severity of symptoms and the histologic lesions tended to increase with larger amounts of antigen used and with longer periods of time before excisions. Histologic examination of the local lymph nodes draining the site of injection, in animals with site excision at one hour, revealed droplets of oil as well as a cellular reaction which commonly occurs about acid-fast bacilli in paraffin oil. In some animals, suggestive changes also occurred in more distant lymph nodes and in the lungs. Site excision at one hour did not prevent the development of tuberculin sensitivity, although the degree of reactivity was higher in animals where the site excision was delayed for a greater number of hours. From these experiments, it would seem that only a small amount of antigen is needed to produce allergic encephalomyelitis. Moreover, enough antigen and adjuvant escapes the site of injection within an hour to reach regional and distant lymph nodes and other organs and there to act as foci of antigenic stimulation. B. S.

Blood ACTH Levels Following Subcutaneous Injections. Lazo-Wasem, E. A., and Hier, S. W.: Proc. Soc. Exper. Biol. & Med. **90**: 380, 1955.

ACTH disappears rapidly from the blood stream. In intact rats the half-life of the ACTH molecule given intravenously is said to be about five minutes and in the adrenalectomized animal much less. In this study, the rate of disappearance of a single subcutaneously administered dose consisting of 10

U.S.P. ACTH units was measured in hypophysectomized male 250 gram rats. At varying intervals, 4 ml. samples of blood were drawn from the abdominal aorta of such animals and injected into the jugular vein of 100 gram hypophysectomized rats. The adrenal ascorbic acid was measured in the recipient animals one hour after the transfusion.

Definite ACTH activity could be detected in the transfused blood samples within a minute after subcutaneous injection. The blood level rose to a peak within four to eight minutes and then fell rapidly for twenty minutes, disappearing completely at eighty minutes. In other studies adrenalectomies were done in the donor rats when the blood samples were taken and the adrenal ascorbic acid depletion was determined. It was found that, in the donor rats, significant depletion of adrenal ascorbic acid does not occur until about twenty-eight minutes after the ACTH has reached its peak in the blood. B. S.

Evaluation of Skin Testing Methods Employed in the Diagnosis of Penicillin Allergy. Tuft, L., Gregory, D. C., and Gregory, J.: Am. J. M. Sc. **230**: 370, 1955.

Because of the present lack of agreement regarding skin testing techniques most suitable for the detection of penicillin sensitivity, the authors investigated the problem in 629 patients. Three groups of patients were studied. The first group consisted of 134 patients who had never received penicillin; the second group consisted of 463 patients who had received penicillin without any known allergic reaction to it; the third group was comprised of 32 patients presenting histories of allergic reactions subsequent to penicillin administration. The test materials employed were: (1) procaine penicillin G in aqueous suspension; (2) dibenzylethylenediamine dipenicillin G in aqueous suspension; and (3) the vehicle used in each of the penicillin preparations (mixture of carboxymethylcellulose, sodium citrate, methylparaben, and propylparaben). For intracutaneous testing, solutions ranging in concentration from 100 units to 300,000 units per cubic centimeter were employed. Scratch tests were performed with concentrations of 10,000 to 300,000 units per cubic centimeter. The only positive skin reaction obtained in the group which had never received penicillin was a mild scratch and intracutaneous response to the 300,000 unit testing solution of procaine penicillin G. The patient was an asthmatic but could not remember ever having received penicillin. Seven individuals in the same group showed very slightly positive reactions to an intracutaneous test with the vehicle. Although 9 patients in Group 2 showed positive reactions following intracutaneous tests with procaine penicillin G, none of them showed a positive response to the scratch tests. Since 3 of these 9 patients manifested positive reactions to the vehicle, there were, in this group, only 6 significant responses to penicillin. In Group 3, there were 3 patients who showed positive reactions to intracutaneous tests with one of the penicillin preparations; one of these patients also had a positive skin reaction to scratch tests with both of the penicillin products employed. This same patients, 17 days later, showed a definite diminution in reaction to both scratch and intracutaneous tests; upon retesting 2 months later, all these reactions were completely negative. The patients in Group 3 were tested at varying intervals following the occurrence of their generalized penicillin reactions; about one-half of them were not tested for at least 2 years following their constitutional reactions. It was significant that 2 of the 3 positive reactors had been tested within 1 month following the occurrence of the penicillin reactions.

Of the entire series of 629 patients, 16 individuals showed slightly positive reactions when tested intracutaneously with the vehicle. In view of this

fact, the authors stress the importance of doing control tests when positive reactions with penicillin are obtained. Comparative tests were done on 2 positive reactors using the following test materials: (1) freshly made penicillin; (2) penicillin prepared 2 months previously and kept under refrigeration; and (3) a 2-month-old solution of penicillin which had not been kept under refrigeration. All reactions were approximately equal in size, which seemed to indicate that for testing purposes penicillin solutions remain quite potent even at room temperatures.

No significant reactions were observed following patch tests with penicillin in patients with previous penicillin reactions, and the authors regard this method of testing to be of significance only in contact allergy to penicillin.

These workers recommend that a 10,000 unit solution be used routinely for intracutaneous testing and that scratch tests should be first performed when a severe sensitivity to penicillin is suspected. The writers conclude that unless skin testing is performed within a short time following the occurrence of a generalized penicillin reaction, the results are likely to yield negative results. They also emphasize the fact that a negative reaction to a skin test does not necessarily exclude the possibility of penicillin allergy, especially if the patient is atopic and has previously received penicillin. R. W.

Allergy to Chicle. Report of a Case and Review of the Literature. Cortés, F. M., and Montiel, J.: Alergia **3**: 41, 1955.

The case of a 12-year-old atopic boy with a history of atopic dermatitis for 9 years and allergic rhinitis, asthma, and urticaria for 6 years is presented. His mother noted that respiratory and dermatologic symptoms were either initiated or aggravated by chewing chicle, caramel, or gum drops, and by the ingestion of the fruit from the chicle tree (*Sapota achras*). As a clinical trial, he was given boiled natural chicle to chew; within a few minutes he developed asthma.

For skin testing, 3 extracts were made from natural chicle: one was prepared from the whole substance; another was prepared from the acetone-soluble fraction; and the third was prepared from the acetone-insoluble fraction. A skin test performed with the 1:100 dilution of the whole chicle extract resulted in a 4-plus reaction and an exacerbation of the dermatitis. Skin tests made with 1:100 dilutions of the acetone-soluble and acetone-insoluble fractions yielded one-plus and three-plus reactions, respectively. Control tests on normal individuals gave negative reactions. Passive transfer studies performed with the patient's serum gave positive reactions to the whole extract and to the acetone-insoluble fraction in all 5 subjects tested. Only one of five passive transfer tests gave positive reactions to the acetone-soluble fraction. Positive skin test reactions were also obtained with 1:100 dilutions of extracts of the chicle fruit, gutta-percha, and gum arabic.

Chicle is composed of 40 per cent resins, 17.4 per cent "gutta" and carbohydrates, 0.6 per cent proteins, and 35 per cent water. Since the resins are soluble in acetone and this fraction was found to have only slight allergenic activity, it is concluded that the main allergenic activity of chicle resides in the "gutta," carbohydrate, and protein fractions. Gutta-percha and chicle are both derived from trees belonging to the Sapotacea family. In view of the positive skin reaction obtained with gutta-percha in this case, an antigenic similarity between these two substances is suggested. CARLOS VIDALES.

Tuberculin Hypersensitivity in Tuberculous Infants Treated with Isoniazid. Robinson, A., Meyer, M., and Middlebrook, G.: New England J. Med. **252**: 983, 1955.

Seven tuberculin-positive infants, ranging in age from 7 to 27 months, who had no roentgenographic evidences of pulmonary involvement received isoniazid in doses of 8 mg. per kilogram of body weight per day. Four became negative to Old Tuberculin in a 1:100 dilution after about eight months' therapy. None of seven infants of similar age who had evidence of pulmonary involvement became tuberculin-negative when similarly treated. This phenomenon had previously been observed only in laboratory animals. It was suggested that BCG vaccine be used in tuberculin-sensitive patients who have lost their sensitivity under antimicrobial therapy. E. W.

Acute Disseminated Encephalomyelitis Treated With ACTH. Report of a Case. Selling, B., and Meilman, E.: New England J. Med. **253**: 275, 1955.

Acute disseminated encephalomyelitis was reported in a 22-year-old nurse who had no previous history of known inciting disease or vaccination. Treatment with ACTH was followed by a prompt remission of symptoms. A mild relapse followed reduction in ACTH dosage and was reversed by another increase in the dosage. Ten months after onset, only mild weakness of the legs and some difficulty in urination remained. It was suggested that clinical and experimental evidence points to the possibility that encephalomyelitis may occur as an expression of hypersensitivity. E. W.

Angioneurotic Edema Caused by Cigarette Filter Tip. Hollander, L.: Arch. Dermat. **72**: 468, 1955.

A patient developed an acute painless swelling of the lower lip during the middle of the night about 4 hours after smoking a filter-tipped cigarette. The swelling lasted for about 12 hours. He had not experienced any discomfort while smoking the cigarette, and recalled that he had not smoked a filter-tipped cigarette in a long time. In order to establish a causal relationship between the filter-tipped cigarette and the angioedema, he smoked another filter-tipped cigarette a few days later. Within a few minutes, he again developed angioedema of the lip after having consumed about one-third of the cigarette. This reaction lasted about 3 hours. On the following day, a similar reaction occurred with a different brand of filter-tipped cigarettes. Since the above episodes, the patient has stopped smoking filtered cigarettes and has had no recurrence of symptoms. R. W.

Anaphylactic Penicillin Reactions: Three Nonfatal Cases of Reaction to Oral Penicillin With Positive Skin Tests and One Fatal Case Following Intramuscular Penicillin. Peters, G. A., Henderson, L. L., and Prickman, L. E.: Proc. Staff Meet., Mayo Clin. **30**: 634, 1955.

Following the administration of penicillin, 4 patients developed anaphylactic reactions, one of which proved fatal. The death occurred in a 69-year-old asthmatic woman who had had a nasal surgical procedure performed and had been given 600,000 units of procaine penicillin intramuscularly postoperatively. She became cyanotic, unresponsive, and died within 20 minutes after the injection, despite emergency measures. An autopsy failed to demonstrate the cause of death. The remaining 3 patients developed episodes of unconsciousness and shock following the use of penicillin troches or tablets. Scratch tests with dilutions of penicillin G produced severe erythema and whealing in 2 patients, one of whom developed a mild constitutional reaction. Positive passive transfer reactions were obtained with some of the sera. It is emphasized that oral penicillin can produce anaphylactic reactions and that potential

reactions to the antibiotic may be detected by a combination of history and skin tests. The authors recommend that a scratch test be performed with a solution containing 10,000 to 20,000 units of penicillin per milliliter or with a drop of the preparation to be given mixed with a drop of saline solution. M. C.

Anaphylactic Shock After Penicillin Injection: Three Fatal Cases. Andersen, A. H.: Ugesk. laeger **117**: 1237, 1955 (Abstract, J. A. M. A. **159**: 1680, 1955).

Anaphylactic shock following the administration of penicillin resulted in death in 3 patients. One of the patients was an asthmatic who had previously experienced a reaction to penicillin. It is stressed that a careful history regarding penicillin sensitivity reactions must be taken before using the antibiotic, that previous allergic reactions should be considered a contraindication of its use, and that the possibility of an anaphylactic shock reaction to penicillin must always be kept in mind. M. C.

Anaphylaxis

Eosinophiles in Passive Anaphylaxis. Redd, L., and Vaughan, J. H.: Proc. Soc. Exper. Biol. & Med. **90**: 317, 1955.

In order to determine whether active antibody production was a prerequisite for the development of eosinophilia, the phenomenon was studied in passive anaphylaxis in guinea pigs. Three times crystallized egg albumen (Ea) was the antigen employed. Rabbit antiserum, with a precipitable anti-Ea N content of 308 μg per milliliter was used for passive sensitization of guinea pigs weighing from 250 to 325 grams. Sensitization was achieved with 23 μg antibody N administered intravenously. The shocking dose of antigen (6 μg Ea N) was given 48 hours later. Total white counts and absolute eosinophile counts were made on peripheral venous blood at fifteen to thirty minutes, and subsequently at 1, 2, 4, 6 or more hours.

Following the shocking dose, a definite eosinophilia was detected in the sensitized animals which was absent in the nonsensitized controls. The rise of eosinophiles was independent of any corresponding rise in the total white blood cell count. The eosinophilia was still present at 6 hours and in some instances at 24 hours.

In other experiments it had been noted that moderate eosinophile responses might be induced in normal guinea pigs with excessive doses of Ea N (160 μg). This did not occur with the smaller doses used in the present experiments. B. S.

Bacterial Allergy Increases Susceptibility to Influenza Virus in Mice. Parfentjev, I. A.: Proc. Soc. Exper. Biol. & Med. **90**: 373, 1955.

The author previously reported that vaccination of mice with *H. pertussis* produced immunity to this organism but lowered the resistance of these animals to various gram-negative bacteria and Shigella endotoxin. In this communication, it is demonstrated that vaccination of mice with *H. pertussis* antigen increases their susceptibility to influenza virus. Mice of different ages were sensitized to *H. pertussis* by intraperitoneal injection of a vaccine and were tested for their susceptibility to influenza virus by intranasal inoculation after an interval of from 5 to 7 days. Death followed in from 5 to 10 days in all mice, but the lethal dose for the sensitized animals was much smaller than that for the controls. Anaphylactic sensitivity to *H. pertussis* nucleo-

protein could be demonstrated in about one-half of the treated weanling mice and in a much greater percentage of sensitized adult mice. However, the increase of susceptibility in the vaccinated animals was not the result of anaphylactic shock, but of diminished resistance to the influenza virus. The autopsy findings showed lesions in the lungs which were typical of an influenza virus infection. Virus inactivated with antiserum in vitro was well tolerated in both normal and sensitized animals. Intraperitoneal injection of antiserum in normal mice gave a high degree of protection against intranasal inoculation of virus. In sensitized mice, however, such pretreatment with antiserum afforded much less protection to the influenza virus. B. S.

Electrocardiographic Changes During Anaphylactic Shock in the Guinea Pig. Canseco, C., Jr., and Ruiz, R. S.: Alergia **3**: 22, 1955.

Electrocardiographic tracings were taken from 10 normal anesthetized guinea pigs. These were compared with tracings obtained from 10 egg-albumin-sensitized guinea pigs during anaphylactic shock. The major alterations in the electrocardiographic tracings noted during shock were increased P-R interval, complete A-V block, bundle branch block, and T-wave changes. These severe alterations of the intracardiac conduction system are believed to be caused by myocardial ischemia and edema, as well as by metabolic changes.
CARLOS VIDALES.

Pharmacology, Physiology, and Pathology

Specificity of the Secondary Response to Protein Antigens. Dixon, F. J., and Maurer, P. H.: J. Immunol. **74**: 419, 1955.

Using relatively pure protein antigens and quantitative immunochemical techniques, the authors studied the specificity of the secondary or anamnestic response in rabbits. They sought to determine (a) the effect of previous immunization with one antigen on the antibody response elicited by the initial injection of a second antigen and (b) the effect of a subsequent immunization with one antigen on the titer of circulating antibody to a previously administered antigen. The antigens studied included human serum albumin, crystalline bovine serum albumin, bovine gamma globulin, canine gamma globulin, crystalline egg albumin, and several others. Some of these antigens were known to show variable degrees of in vitro cross reactivity with the antisera of other similar antigens. Human and bovine gamma globulins showed a much greater tendency to cross reactivity than the albumins of the same species. Most of the present experiments were run with serum albumin antigens because of their greater purity as well as their weaker tendency to cross reactivity. Antibody determinations were made by commonly employed quantitative immunochemical precipitation techniques, by the "P_{80} Method" of measuring the ability of antisera to precipitate I^{131}-labeled antigen or by capillary precipitin ring tests. The immune response was also evaluated on the basis of the rate of elimination of the antigens during the primary and secondary antibody responses. It had been shown that, in the primary responses to heterologous serum antigens, the globulins were eliminated within 7 to 8 days and the albumins within 10 to 14 days but, in the secondary responses, all serum protein antigens were eliminated within 4 to 5 days.

The results of the present studies showed that the previous immunization of rabbits with one antigen commonly increased the initial antibody response to a second antigen when the antigens were related. It was also shown that rises in antibody titers to a previously administered protein antigen occurred following a subsequent stimulation with a second antigen, but this occurred

only when the antigens were related. Despite only a limited antigenic similarity of the antigens employed, the production of the entire spectrum of antibodies to the originally administered antigen could be stimulated by the subsequent injection of a second slightly related antigen. Totally unrelated antigens could not reproduce these phenomena. The authors discuss at length the possible explanations for the apparent lack of specificity of some of the secondary responses in the above experiments. B. S.

Studies on the Transfer of Lymph Node Cells. V. Transfer of Cells Incubated in Vitro With Suspension of Shigella Paradysenteriae. Harris, S., and Harris, T. H.: J. Immunol. **74**: 318, 1955.

In their previous studies, the authors had found that washed cells of popliteal lymph nodes which were draining the sites of injection of dysentery bacilli in rabbits were responsible for the appearance of agglutinins to dysentery bacilli in recipient animals within a few days after injection. The various factors influencing this phenomenon were studied. Cells obtained from the draining lymph nodes as early as ten minutes after the injection of antigen into the donor's tissues were capable of reproducing the phenomenon. The experimental findings suggested the possibility that *in vivo* contact between lymph node cells and the antigen might not be essential for the demonstration of this phenomenon. Experiments were undertaken to determine whether *in vitro* contact of normal lymph node cells and bacilli would be sufficient. In other experiments, normal lymph node cells and bacilli were injected separately into the veins of normal animals. In most experiments, irradiated recipients were used in the attempt to suppress early active antibody production.

Four days after the injection of washed popliteal and axillary lymph node cells which had been incubated *in vitro* with dysentery bacilli, agglutinin appeared in the sera of irradiated recipients. Similar findings were obtained in irradiated recipients which had received separate intravenous injections of cells and organisms. With heated aliquots of cell suspensions, antibodies usually did not appear before the eighth day after transfer.

The number of organisms injected into recipients in the various cell transfer experiments was found to be insufficient to induce active agglutinin formation in irradiated animals within 12 days. Some recipients in the cell transfer experiments received, in addition, subcutaneous injections of typhoid bacilli within an hour after the lymph node cells were administered. Irradiated recipients of heated lymph node cells usually developed no typhoid agglutinins during the first 12 days. However, irradiated recipients of untreated lymph node cells developed agglutinins during the first week after transfer in 70 per cent of animals.

When untreated splenic cells which were incubated *in vitro* with dysentery bacilli were injected into irradiated recipients, agglutinins appeared on the fourth day, as when lymph node cells were used. When thymus cells were similarly employed, no agglutinins were found. B. S.

The Sympathomimetic and Other Pharmacological Properties of DL-(1,2,3,4-Tetrahydro-1-Naphthyl)-Imidazoline (Tetrahydrozoline). Hutcheon, D. E., P'an, S. Y., Gardocki, J. F., and Jaeger, D. A.: J. Pharmacol. & Exper. Therap. **113**: 341, 1955.

Tetrahydrozoline (Tyzine), injected intravenously, sharply increased the arterial blood pressure in cats and dogs. The duration of pressor response was very similar to that produced by naphazoline (Privine). The duration

of effect was variable, the first dose sometimes producing a short-lived effect compared to subsequent ones. Variable pressor responses were obtained when Tyzine was given orally. The pressor response was diminished but never reversed by adrenolytic agents. A dose of 1 ml. of a 1 per cent solution intranasally in dogs failed to affect systemic blood pressure. Tyzine in a perfusate constricted the vessels of the isolated rabbit ear in doses as small as 0.2 μg. It reduced the rate of blood flow in the hind limb of a dog. Tyzine prolonged the duration of local anesthesia when it was mixed with procaine and injected intracutaneously. Both tetrahydrozoline and naphazoline slowed the heart rate in anesthetized cats and dogs, an effect only partly counteracted by bilateral vagotomy. Animals made susceptible to ventricular arrhythmias by the drug, harman methosulfate, failed to show arrhythmias when Tyzine was injected intravenously immediately thereafter. The perfused cat's heart showed no change in contractile force or rate or in coronary vasoconstriction upon the addition of Tyzine in doses up to 0.25 mg. Tetrahydrozoline caused prolonged contraction of the nictitating membrane of cats and markedly decreased the tone and rhythm of cat intestine. The guinea pig tracheal chain preparation was not relaxed by this drug, although histamine-induced contractions of this chain were inhibited. Tyzine prolonged the hypnotic effect of sodium pentobarbital. An increase in blood sugar, comparable to the hyperglycemia induced by naphazoline, was noted. The toxicity of Tyzine was less than that of naphazoline in rats and mice. Ciliary movement of tracheal rings in rats was not inhibited by 0.1 to 0.2 per cent of Tyzine in Locke's solution, although slight suppression was noted at a concentration of 0.4 per cent.

E. K.

Prevention of Eosinopenia in Adrenalectomized Dogs by an Antihistaminic Drug. Swingle, W. W., Eisler, M., Baker, C., LeBrie, S. J., and Brannick, L.: Am. J. Physiol. **182**: 256, 1955.

Nontoxic doses of Pyribenzamine were shown to prevent the expected eosinopenic reaction in adrenalectomized dogs subsequent to the administration of adequate doses of histamine, Pituitrin, epinephrine, 48-80, Regitine, Apresoline, and Metrazol. All these drugs have been shown to be markedly eosinopenic in the adrenalectomized dog. In addition to preventing the eosinophile drop, the antihistamine appeared to eliminate or ameliorate many of the toxic effects ordinarily produced by these drugs. When the experimental dogs were injected with cortisone (free alcohol), Pyribenzamine failed to interfere with the expected eosinopenia. These results appear to indicate that stress-induced eosinopenia in adrenalectomized dogs is due to the histamine-releasing action of the drugs in this experiment.

H. F.

Changes in Blood Leucocytes Resulting From an Antigen-Antibody Reaction. Hartman, J. D., and Hoch, W. S.: Am. J. Physiol. **183**: 214, 1955.

When the bloods of normal guinea pigs and of guinea pigs sensitized with egg albumin were exposed in vitro to this antigen, certain cytologic changes were observed under contract phase microscopy. These changes consisted of leucocyte clumping, intracellular vacuolation, and a certain amount of cellular destruction. There was a concomitant drop in the leucocyte count. Although these changes appeared in the bloods of both normal and sensitive animals, the manifestations of leucocyte damage were significantly greater in the blood from sensitized animals. These findings seem to indicate that the antigen-antibody reaction has an injurious effect upon blood leucocytes.

H. F.

Studies in Eczematous Sensitizations. V. The Role of the Regional Lymph Node. Rostenberg, A., Jr., and Best, W. R.: Arch. Dermat. **72**: 221, 1955.

In 8 guinea pigs, the right groin was painted with a 10 per cent solution of 2,4-dinitrochlorobenzene in acetone. The animals were divided into 4 groups of 2 each. A right inguinal lymph node was removed from each animal, the groups being operated upon on the first, third, fifth, and ninth days, respectively, after the application of the dye. Six additional guinea pigs were exposed in an analogous fashion to a 25 per cent solution of croton oil, and the nodes were removed at similar intervals. Three weeks later, the same procedure of application and node excision was repeated on each pig of both groups, using the left side. Each animal was tested for development of sensitivity to 2,4-dinitrochlorobenzene and croton oil at the time of the second biopsy. The testing strength of 2,4-dinitrochlorobenzene was a 1-1,000 solution in acetone and the croton oil was used in its original strength. Four of the pigs treated with 2,4-dinitrochlorobenzene and 2 of those exposed to the croton oil died before the second application could be made. Two animals showed an eczematous sensitivity to 2,4-dinitrochlorobenzene, but none developed a sensitivity to the croton oil.

Each lymph node was bisected, and touch imprints were made from the exposed surfaces on 2 clean glass slides. The slides were then coded so that the cells could be studied impartially by various investigators. They were classified according to the cells observed, with the following 9 types being identified: (1) reticuloendothelial, (2) immature lymphocyte, (3) medium and mature lymphocytes, (4) monocyte, (5) plasma, (6) segmented neutrophile, (7) eosinophile, (8) basophile, and (9) atypical granular. Medium and mature lymphocytes predominated in almost all the slides. Occasionally, large numbers of segmented neutrophiles or eosinophiles were observed. No important trends were observed suggesting any changes characteristic of an immunologic response. The authors conclude that the regional lymph node does not appear to be an important factor in the development of an eczematous sensitivity to a simple chemical. R. W.

Mechanism of Antibody-Antigen Reaction. Najjar, V. A., and Fisher, J.: Science **122**: 1272, 1955.

Rabbits were injected subcutaneously at various intervals with 10 mg. of yeast crystalline alcohol dehydrogenase and then bled. The resulting sera were mixed with antigen-antibody complexes which had been prepared from the pooled sera obtained from similarly immunized rabbits. Original antigen was then added to the supernates. Despite this selective and exhaustive absorption with a particular complex, some antibodies which reacted only with the original antigen remained in the supernate. In a similar experiment, absorption was accomplished by the addition of 2 types of complexes but antibodies were detected in the supernate that reacted only with the original antigen. On the basis of these and other experiments, it was suggested that the "univalent" or incomplete" antibody has the characteristics of an antibody to the complex. According to this concept, an antigen, when first introduced into the body, stimulates specific antibody formation. Further contact of antigen with antibody results in the formation of an antigen-antibody complex. The configuration of the antigen and antibody is mutually altered and the complex behaves as a new antigen. Specific antibodies are then formed against the complex. With repeated introduction of the original antigen into the system, additional complexes are formed. M. C.

Miscellaneous

Autoerythrocyte Sensitization. A Form of Purpura Producing Painful Bruising Folllowing Autosensitization to Red Blood Cells in Certain Women. Gardner, F. H., and Diamond, L. K.: Blood **10**: 675, 1955.

The authors studied four female patients who developed abnormal responses following bruising. Their symptoms consisted of local pain, swelling, and extension of bleeding into adjacent areas, often to a serious degree. These women were observed over a period of 20 years. Two were 19 years old when the initial ecchymotic lesion occurred; the other two were 24 and 40 years old, respectively. Two of the women also had signs of systemic bleeding; splenectomies had been performed on two of the patients in an attempt to control the hemorrhagic tendency. Each patient had numerous episodes of severe, painful, swollen lesions following bruising. Autohemotherapy appeared to relieve one patient, but similar treatment or attempts at hyposensitization with red cell stroma provoked constitutional reactions in the other three patients. These three patients experienced not only severe ecchymotic reactions at the site of the injection, but also had nausea, vomiting, and left upper quadrant pain, suggesting a possible acute splenitis, shortly after receiving the injection. Cortisone produced marked subjective improvement in one patient when a trial course was given.

Routine hematologic studies on each patient were within normal limits. Within 24 or 48 hours following an intracutaneous test with 0.1 c.c. of autogenous washed red cells or red cell stroma, each patient developed a painful, swollen, ecchymotic lesion varying in size from 2 by 2 cm. to 10 by 10 cm. A similar response was provoked by the stroma of red cells from normal donors. The size of the reactions obtained on skin testing closely paralleled the concentration of hematocrit in the test solutions. Normal control subjects failed to show similar responses to all these skin tests. Hemoglobin, plasma, serum, and plasma fractions employed for skin testing produced negative reactions on the four patients and on the control subjects.

The antigenic factor of the red cell was present in the stromal lipoproteins and not in the hemoglobin. These patients appeared to develop abnormal reactions to their own red cells, when they extravasated into extravascular tissues, and a certain concentration of red cells seemed necessary to initiate the tissue reaction. The authors postulate that a fixed tissue antibody reacts with red cell stroma to produce edema, increased capillary permeability, and further extravasation of blood into the tissues. The lesion continues to spread by further contact of the red cells at the periphery with sensitized tissue. They suggest that the accumulation of extravascular tissue fluid finally decreases the red cell concentration below the threshold necessary for the occurrence of the reaction. The unusual manifestations of purpura observed in these four female patients suggest an "autosensitization by the patients to their own blood." R. W.

Nonbacterial Regional Lymphadenitis ("Cat-Scratch Fever"). An Evaluation of the Diagnostic Intradermal Test. McGovern, J. J., Kunz, L. J., and Blodgett, F. M.: New England J. Med. **252**: 166, 1955.

Antigens were prepared from the suppurative material obtained from the lymph glands of 3 patients suffering from "cat-scratch fever." The purulent material was diluted 1 to 5 in 0.85 per cent sterile sodium chloride solution and heated for an hour on two consecutive days in a water bath at 56° C. Eighteen patients with "cat-scratch fever" were tested intracutaneously with 0.1 c.c. of one or more of the three antigens or with a pool of the three anti-

gens. An immediate reaction, consisting of a wheal and flare, usually developed within 10 minutes and persisted for as long as 24 hours in most cases. In all cases, however, this nonspecific reaction had disappeared 48 hours after inoculation. A reaction was considered to be positive if there was an indurated papule measuring 4 mm. or more surrounded by a zone of erythema about 1 cm. or more in diameter. The test sites were read in 24 and 48 hours. In patients in whom positive reactions were not observed at 48 hours, it was often impossible to determine the site of inoculation. Of 18 patients with nonbacterial regional lymphadenitis tested with this antigen, all responded with positive skin reactions. Of 38 subjects, members of families of patients with nonbacterial regional lymphadenitis, 4 (10.5 per cent) showed positive reactions. Of 21 subjects in whom there was no known history of nonbacterial regional lymphadenitis and who were not members of the patients' families, one, or 4.8 per cent, showed a positive reaction. When the personnel of an animal hospital was tested, 4 of the 18 tested (22.2 per cent) had positive skin reactions in contrast to a single positive reaction encountered among 22 employees of a general hospital tested with the same antigen. There was, therefore, a definite indication that high-risk conditions for nonbacterial regional lymphadenitis existed in the families of those who had the disease, as well as in employees of animal hospitals. It was concluded that the demonstration of positive reactions with skin-testing material, as now prepared, has little diagnostic value in the absence of well-defined clinical signs and symptoms. E. W.

Observations on the Antibody Content of the Blood in Patients With Multiple Myeloma. Lawson, H. A., Stuart, C. A., Paull, A. M., Phillips, A. M., and Phillips, R. W.: New England J. Med. **252**: 13, 1955.

The blood of nine patients with multiple myeloma was investigated for antibody titers. The antibodies studied were agglutinins for *Salmonella typhosa, Paracolobactrum ballerup, Escherichia coli,* sheep erythrocytes and type-specific agglutinins for human A and B erythrocytes, lysins for *S. typhosa* and *Esch. coli,* and sheep cell (amboceptor). The titers of these patients were compared with those of normal subjects or with patients suffering from other diseases. Four of the nine patients with multiple myeloma showed no antibodies, including the blood-group antibodies, two on the initial examination and two on subsequent examinations. In the remaining five patients only a single examination was possible. Although some antibodies were present in the serum of these five patients, in only one case was the titer considered to be at normal level. Not every normal person or control patient had every one of the antibodies included in this investigation, but a complete absence of all antibodies or a lack of the appropriate isohemagglutinins was observed only in patients with myelomatosis. Amboceptor was not detected at any time in the serum of the nine patients with mutliple myeloma, although it was present in 97 per cent of controls. Analysis of serum proteins by filter-paper electrophoresis was done in five patients, all of whom demonstrated a deficiency of antibodies. Four showed a high peak of gamma globulin and the fifth a tall peak representing the so-called M component. This patient with the peak M component had a complete absence of gamma globulin, which was revealed by electrophoretic analysis. He was, however, remarkably free from infection in contrast to patients with agammaglobulinemia. "The immunologic abnormality demonstrated in multiple myeloma is considered to be the result of abnormal function of the malignant plasma cells whereby deranged protein synthesis results in the production of abnormal proteins at the expense of normal proteins, including antibody protein." E. W.

Inhibition of the Apomorphine-Induced Vomiting Syndrome by Antihistaminic Agents. Boyd, E. M., Cassell, W. A., Boyd, C. E., and Miller, J. K.: J. Pharmacol. & Exper. Therap. **113**: 299, 1955.

Thirty-one antihistaminic agents were screened for antemetic activity. Varying doses of a specific antihistamine were administered to 5 dogs orally 2 hours before the intramuscular injections of an emetic dose of apomorphine. One dog served as a control. This study was repeated at 2- to 7-day intervals, with the same dogs receiving each of the series of antihistamines. It was found that 22 antihistaminics inhibited the frequency of retching at the statistical probability level of 0.05 or less and 11 antihistaminics inhibited retching at the level of 0.01 or less. The antemetic doses were from one-tenth to one-half or higher of the minimal toxic dose. The effective doses ranged from 10 to 40 times the usual human dose. An analysis is presented of the molecular configurations which relate to antemetic activity. E. K.

Occurrence of the "L.E." Phenomenon in a Patient With a Severe Penicillin Reaction. Paull, A. M.: New England J. Med. **252**: 128, 1955.

A 64-year-old white male with a long-standing history of chronic bronchitis, pulmonary emphysema, pulmonary fibrosis, bronchiectasis, cor pulmonale, hypertensive and arteriosclerotic heart disease, and diabetes mellitus was admitted to the hospital with pneumonia and congestive heart failure. The laboratory findings on admission were compatible with congestive heart failure, but examination of the peripheral blood for "L.E." cells revealed the presence of these cells. The patient was treated with digitalis, mercurial diuretics, phlebotomies, penicillin, and streptomycin, made an uneventful recovery, and was discharged. Some time later, he was readmitted with drug sickness manifested by an urticarial rash, arthralgias of the knees, ankles, shoulders, and wrists, and a high fever. The peripheral blood was again examined and found to contain "L.E." cells (low-grade positive). The patient was treated with ACTH and made a rapid recovery. When repeated examinations of the peripheral blood were made on his follow-up visits to the hospital, no "L.E." cells were found. The author states that it is highly probable that an immunologic mechanism was responsible for the "L.E." phenomenon which was observed in his patient with the severe penicillin reaction. E. W.

A Study of Illness in a Group of Cleveland Families. VIII. Relation of Tonsillectomy to Incidence of Common Respiratory Diseases in Children. McCorkle, L. P., Hodges, R. G., Badger, G. F., Dingle, J. H., and Jordan, W. S., Jr.: New England J. Med. **252**: 1066, 1955.

Among 230 children over the age of 3 years who were observed from 1948 to 1952, the rates of incidence for the common respiratory diseases were similar among children of comparable ages who had had tonsillectomies and among those who had not. Among 26 children who had a tonsillectomy while under observation, a higher than expected rate of common respiratory diseases, both before and after operation, was found. Tonsillectomy did not materially alter this incidence. E. W.

Tropical Eosinophilia: Report of Two Cases Occurring More Than a Year After Departure From India. Dalrymple, W.: New England J. Med. **252**: 585, 1955.

Two cases of tropical eosinophilia were observed in patients who had been away from India for more than a year. The first patient, a young man who

had been in India 34 months previously, complained of mild wheezing respirations, right lower quadrant pain, a dry cough, and a node in the right axilla. Throughout his illness he had blood eosinophilia which ranged between 12 and 71 per cent. X-ray of his chest on one occasion was normal and on another showed a questionable nodularity throughout the lung fields. Following treatment with oxophenarsine hydrochloride in doses of 325 mg. intravenously every 5 days, there was rapid disappearance of his asthma and eosinophilia. The second patient, also a young man with similar complaints, had been back from India for 14 months. X-rays of his chest, however, were repeatedly normal. His blood eosinophilia ranged from 7 to 50 per cent. He received 9 intravenous doses of oxophenarsine hydrochloride over a period of 5 weeks. His eosinophilia, wheezing, and cough promptly disappeared. Follow-up of both patients 7 months after treatment indicated that they were in good health. E. W.